

Figure 1 Commonly used glycosylating agents

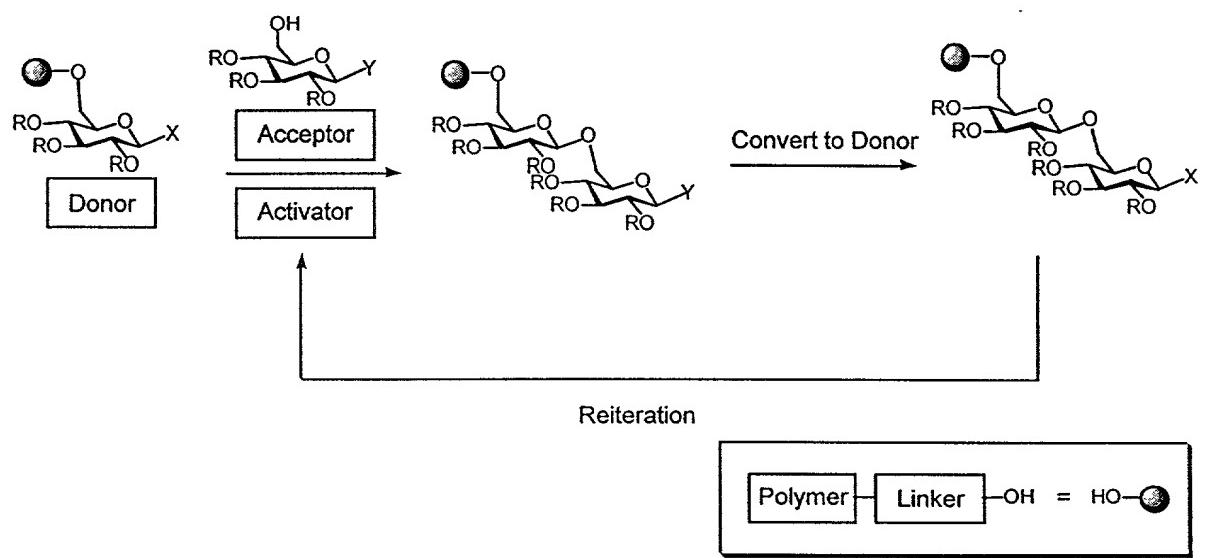


Figure 2 Donor bound solid-phase carbohydrate synthesis

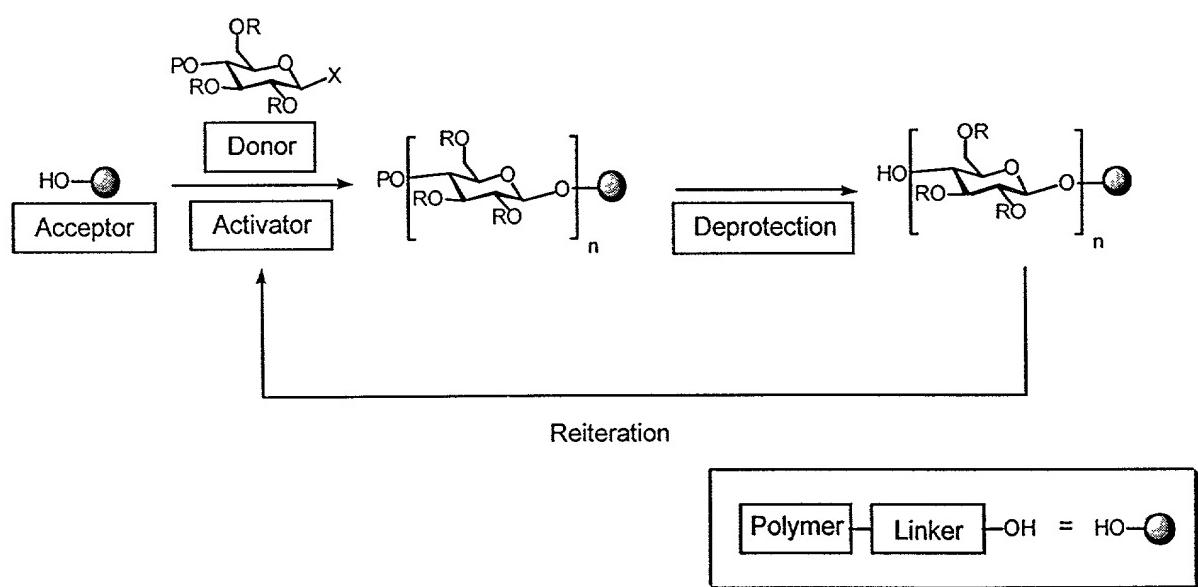
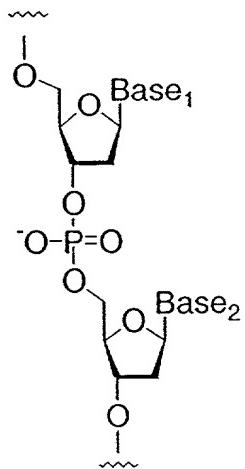


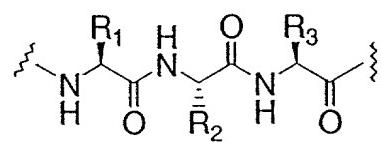
Figure 3 Acceptor bound solid-phase carbohydrate synthesis

Figure 4

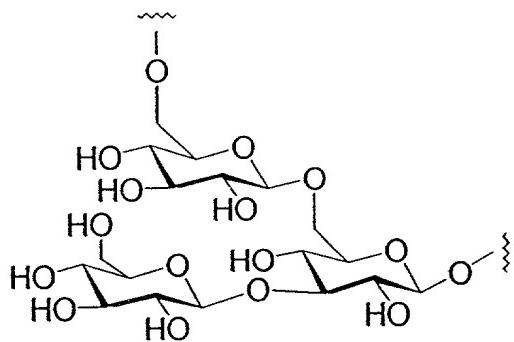
a) oligonucleotides



b) oligopeptides



c) oligosaccharides



Automated Oligosaccharide Synthesizer

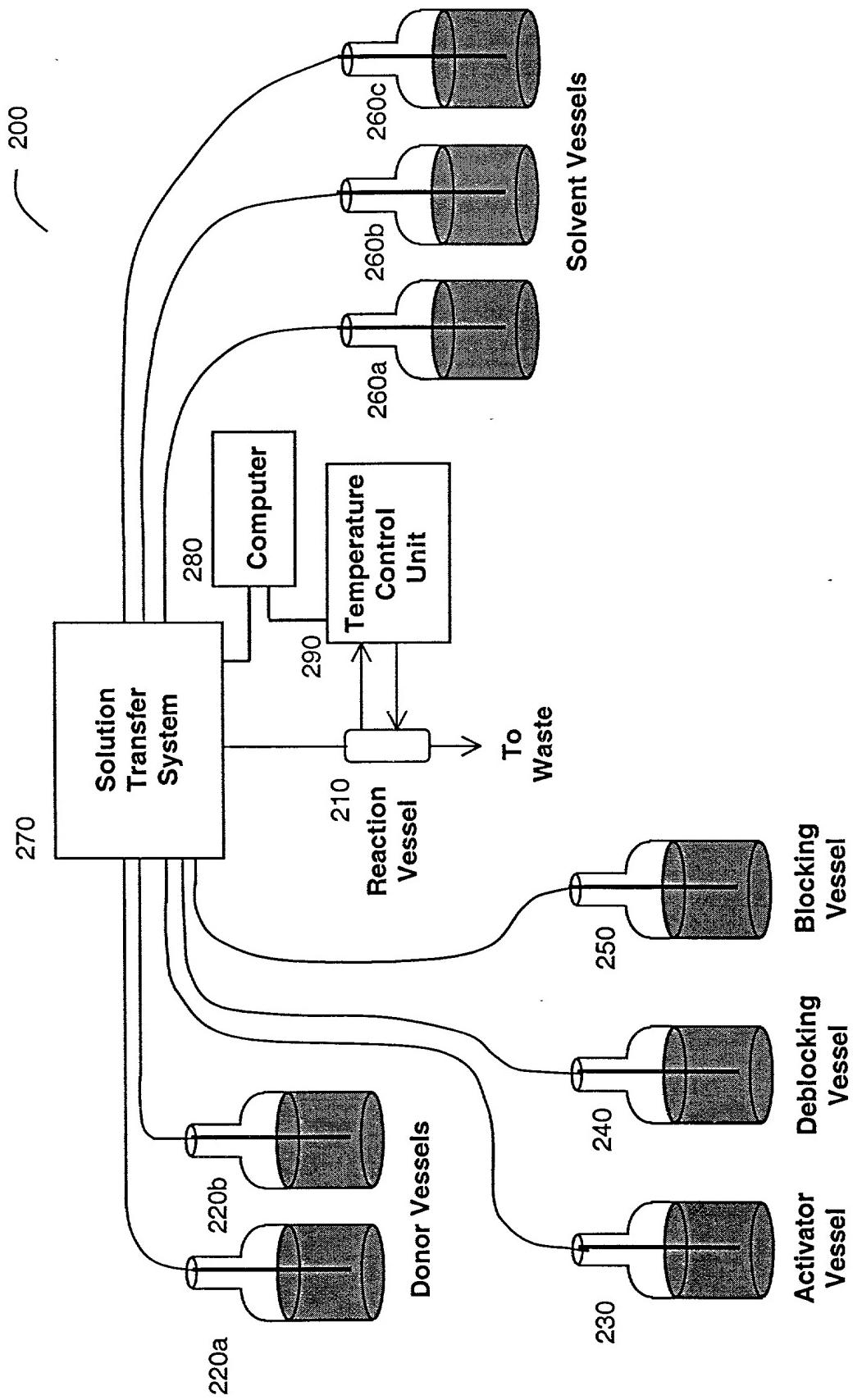


Figure 5

Automated Oligosaccharide Synthesizer

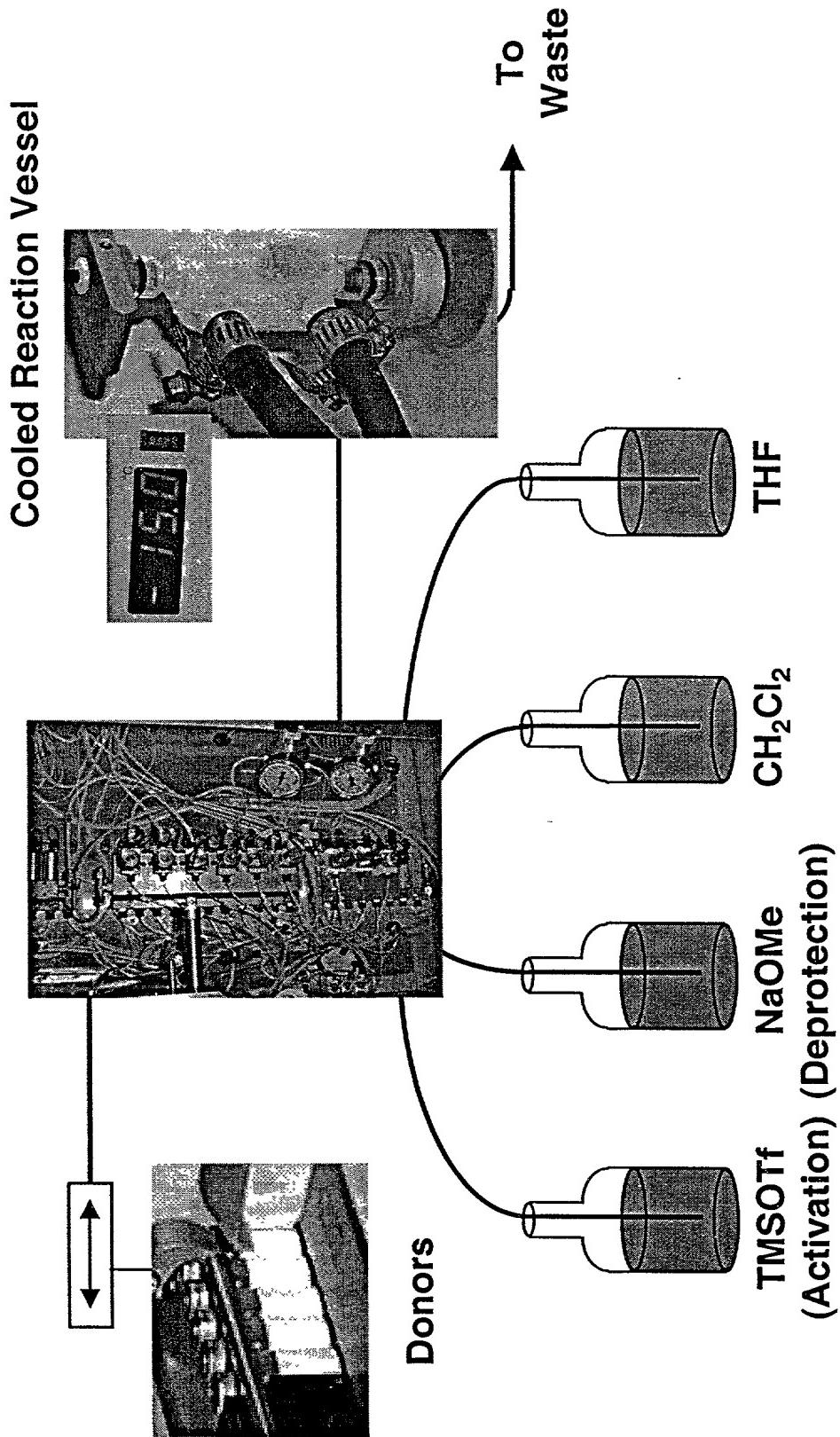


Figure 6

Double-Walled Cooled Reaction Vessel

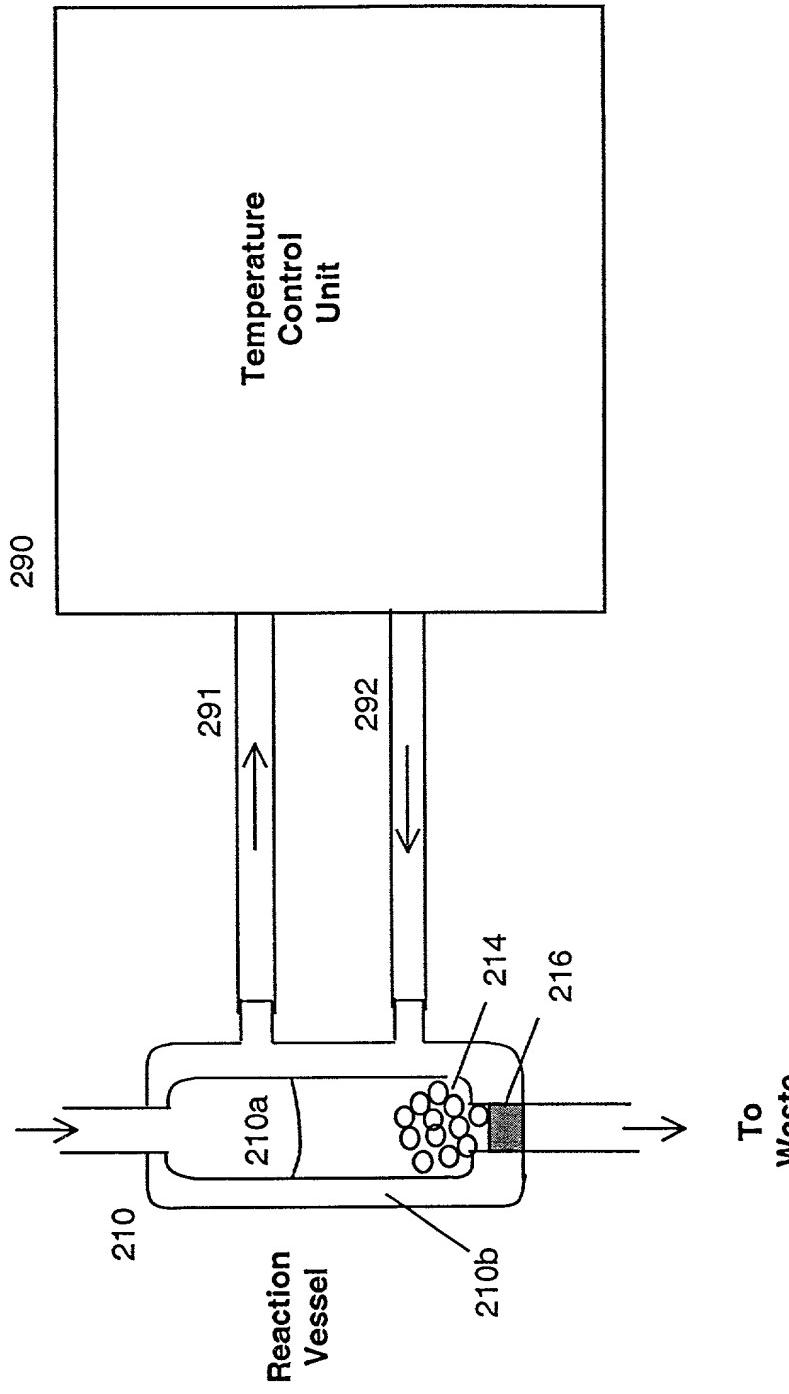
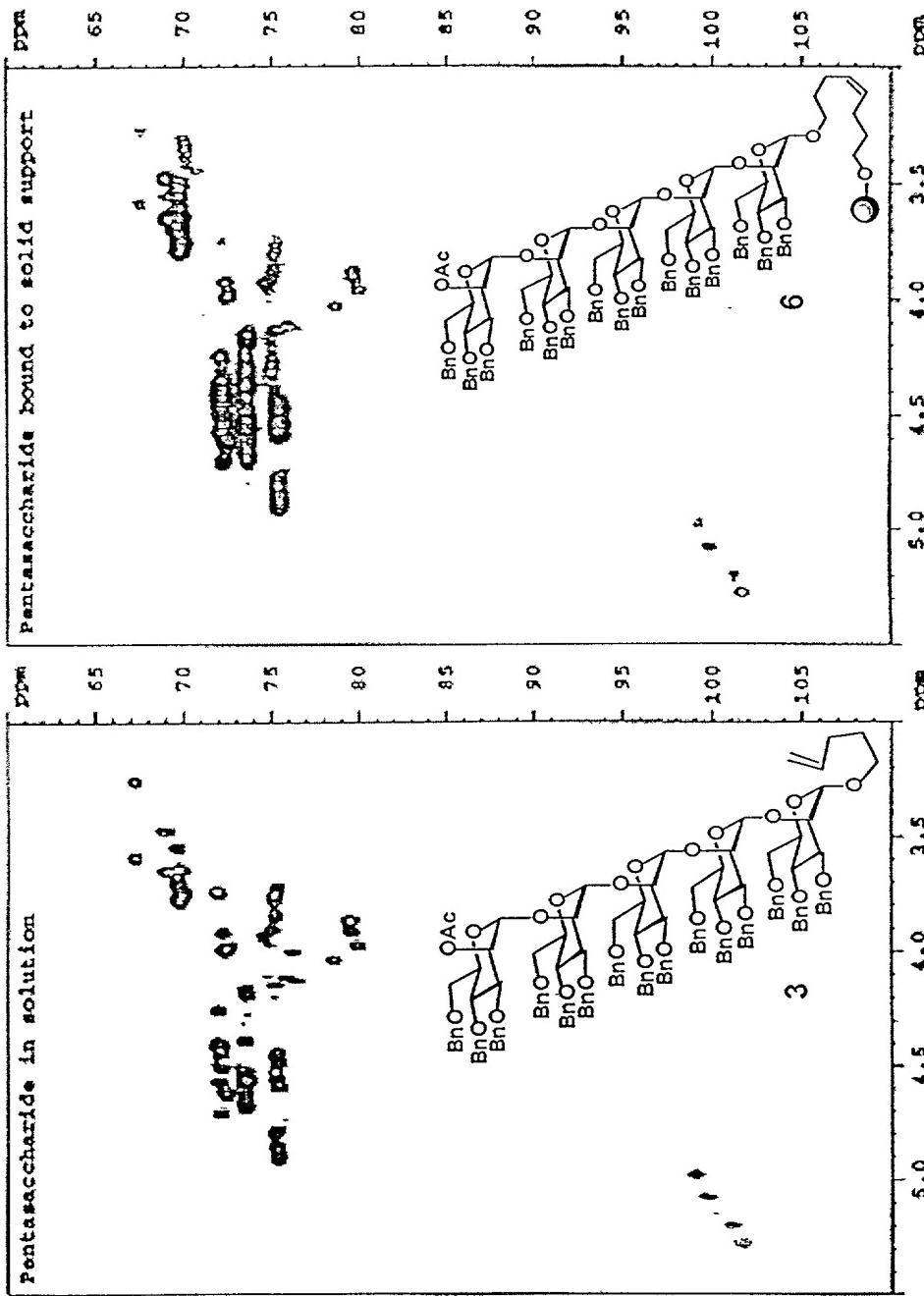


Figure 7

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Figure 8

2D-NMR comparison of resin bound and solution phase pentamer



Automated Synthesis of the Phytoalexin Elicitor β -Glucan Using Glycosyl Phosphates

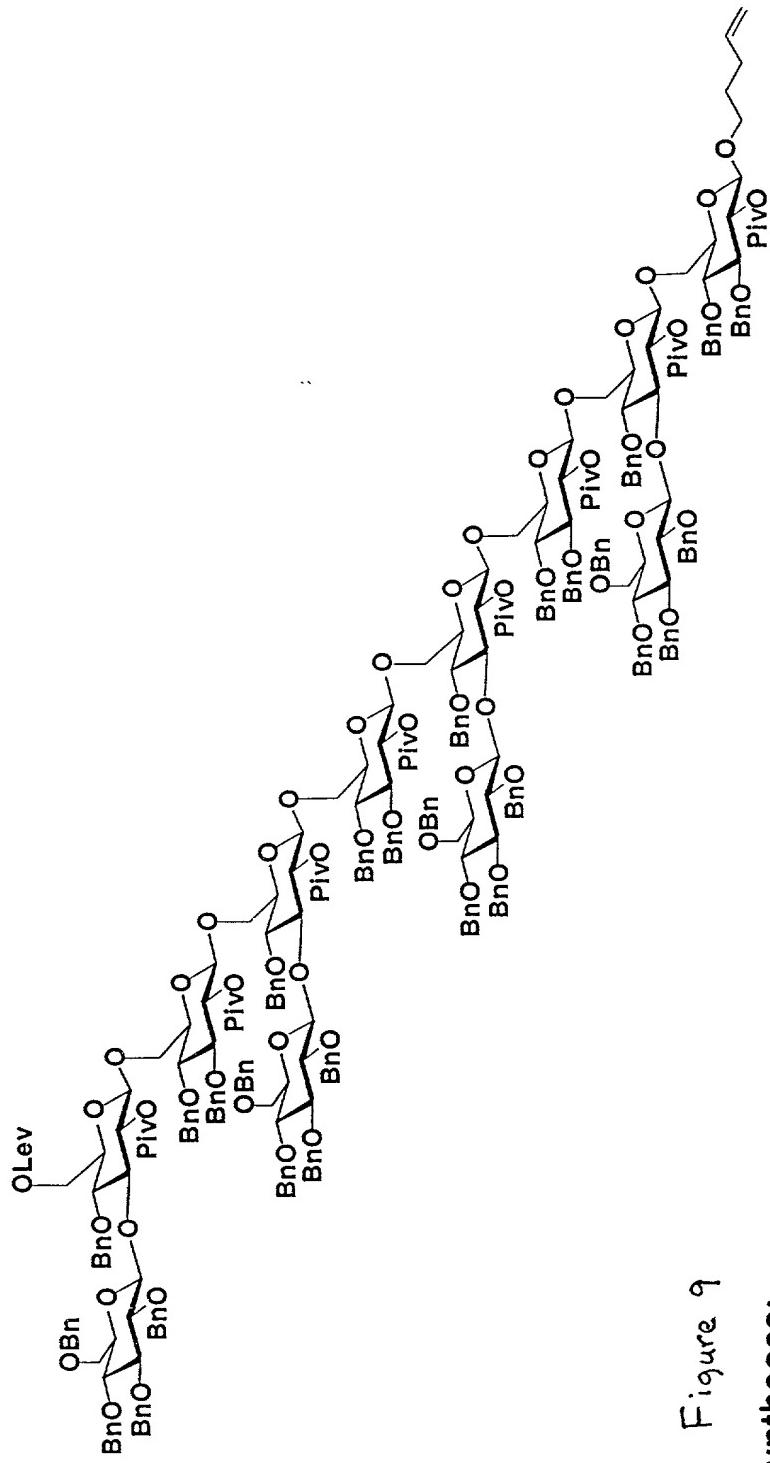


Figure 9

Prior syntheses:

Garegg et al. *Angew. Chem. Int. Ed.* 1983, 22, 793;
van Boom et al. *Chem. Eur. J.* 1995, 1, 16;
on soluble support: van Boom et al. *Recl. Trav. Chim. Pays-Bas* 1993, 112, 464;
on polymer support using trisaccharide blocks: Nicolaou et al. *Angew. Chem. Int. Ed.* 1998, 37, 1559.

Figure 10

Automated Oligosaccharide Synthesis

Chemical Issues:

- Choice of Resin (Merrifield's, Argopore, Tentagel)
- Linker: 
- Glycosylation Protocol
- Deprotection Protocol
- Capping Cycle
- Cleavage Method
- Purification Technique

Practical Issues:

- Scale ($\mu\text{mol}\text{-mmol}$)
- Cycle Development/Time
- Temperature Control Device

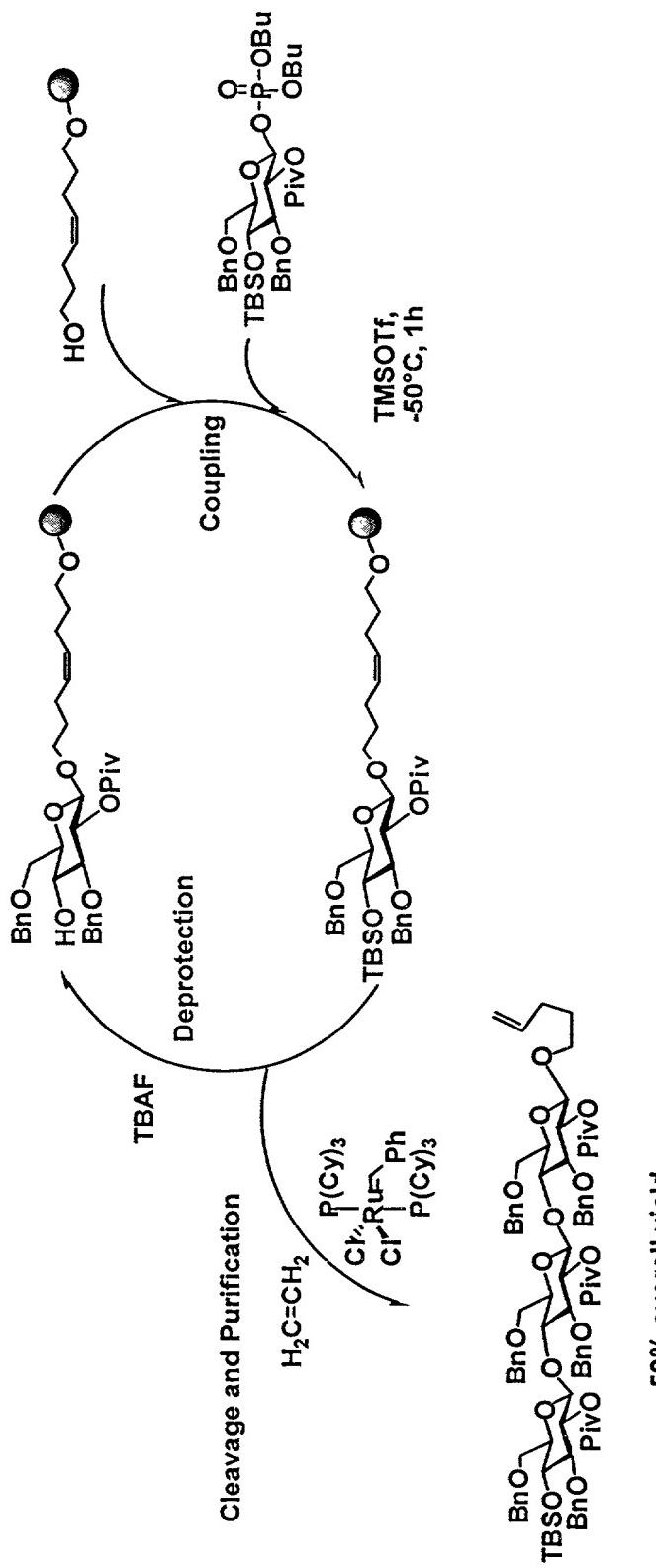
Automated Oligosaccharide Synthesis with Glycosyl Phosphates: Coupling Cycle

	Reagent/Solvent	Equivalents	Temperature	Time	
→ Coupling	Donor TMSOTf	5 5	-15 °C	15 min	
Washing	CH ₂ Cl ₂ THF			5 min	
Coupling	Donor TMSOTf	5 5	-15 °C	15 min	
Washing	CH ₂ Cl ₂ THF			5 min	
Deprotection	N ₂ H ₄ -HOAc		15 °C	30 min	
Washing	Pyr./AcOH			5 min	
Deprotection	N ₂ H ₄ -HOAc		15 °C	30 min	
Washing	Pyr./AcOH			5 min	
					Cycle Time per residue 110 min

Figure 11

Figure 12

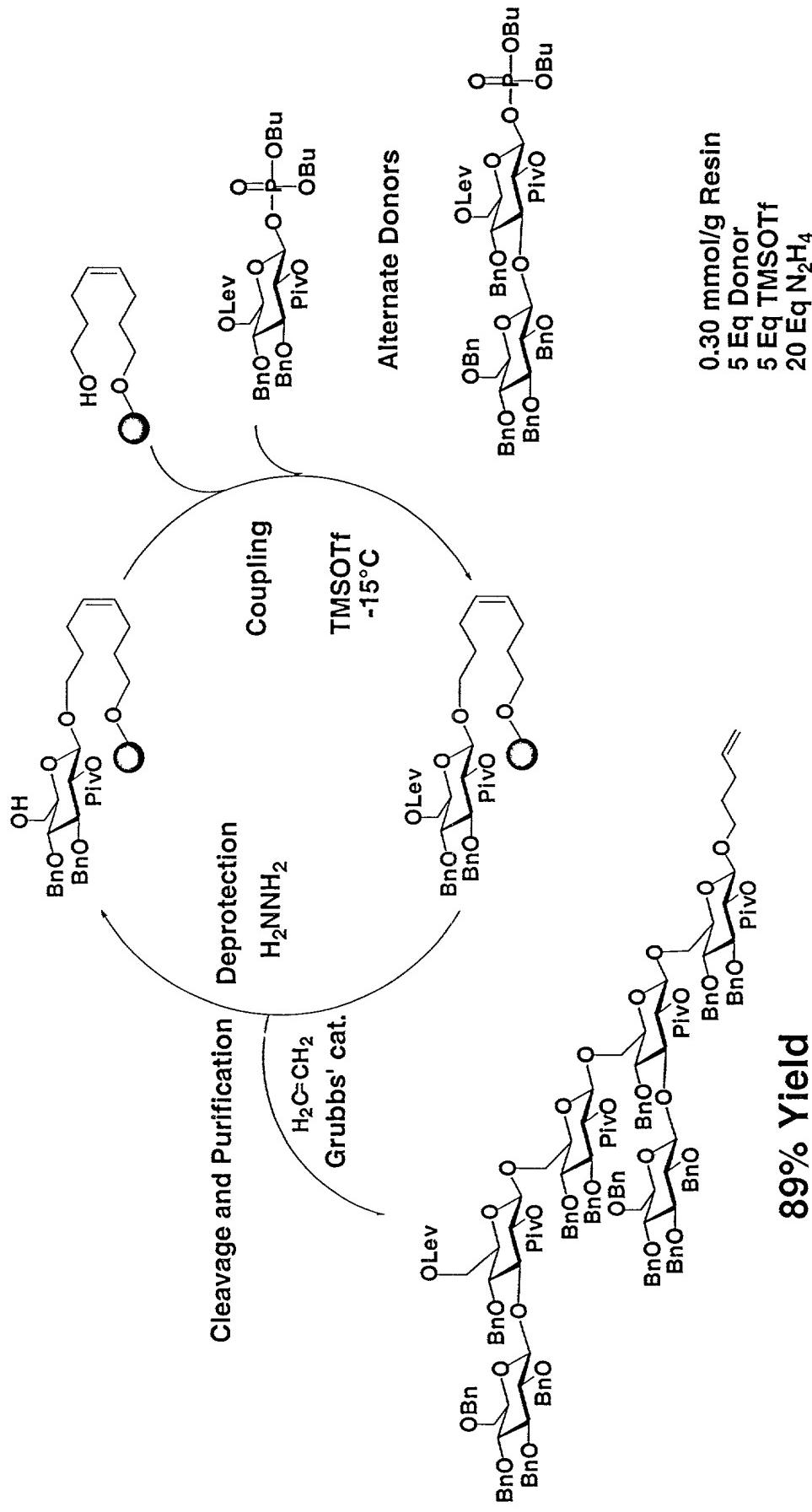
Solid Support Oligosaccharide Synthesis: Glycosyl Phosphate Donors



- Advantages:**
 - excess reagents drive reactions to completion
 - purification only at the end of the synthesis

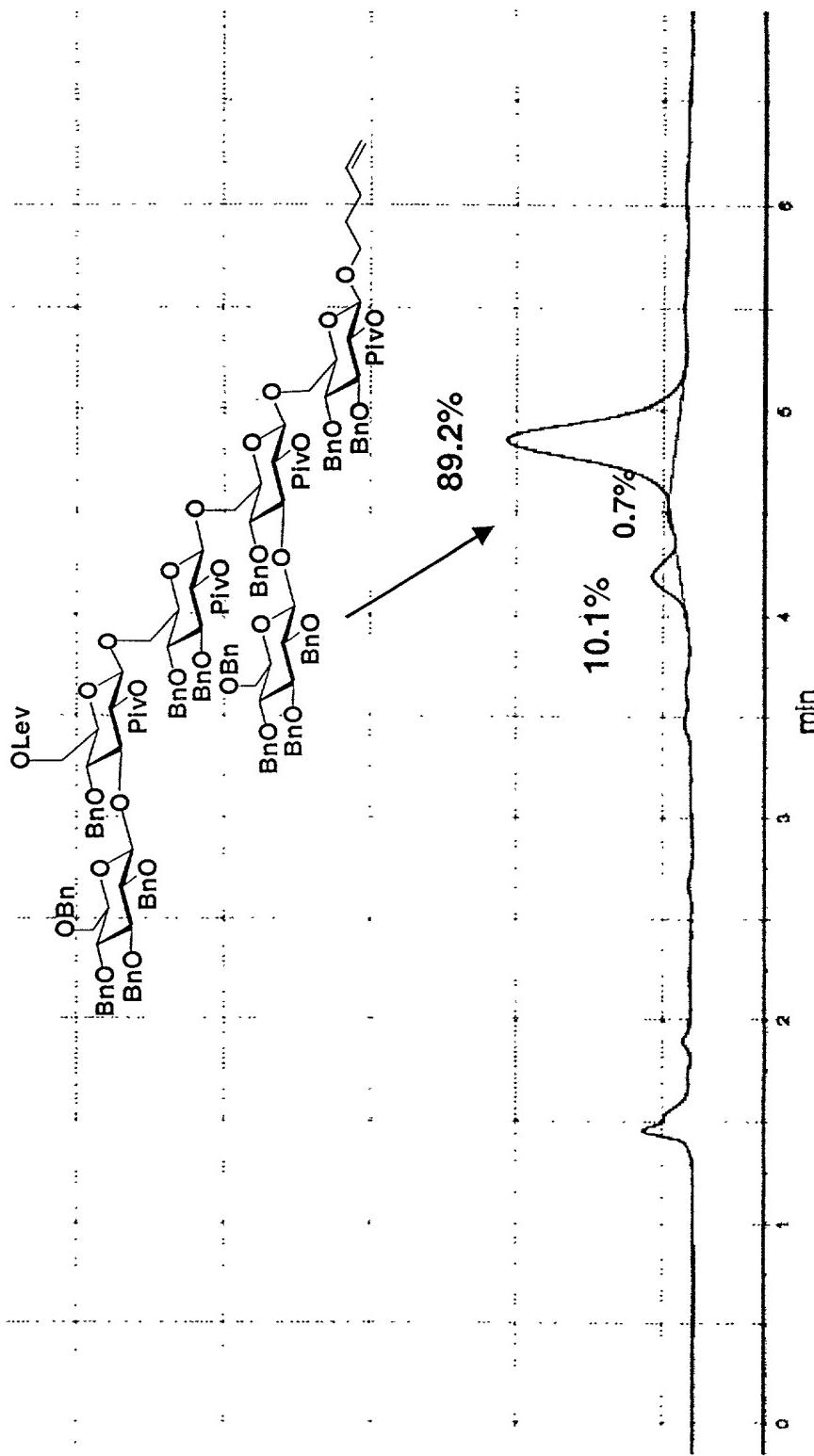
Figure 13

Automated Hexasaccharide Synthesis Using Glycosyl Phosphates



Crude HPLC Profile of the Hexamer Synthesis

Figure 14



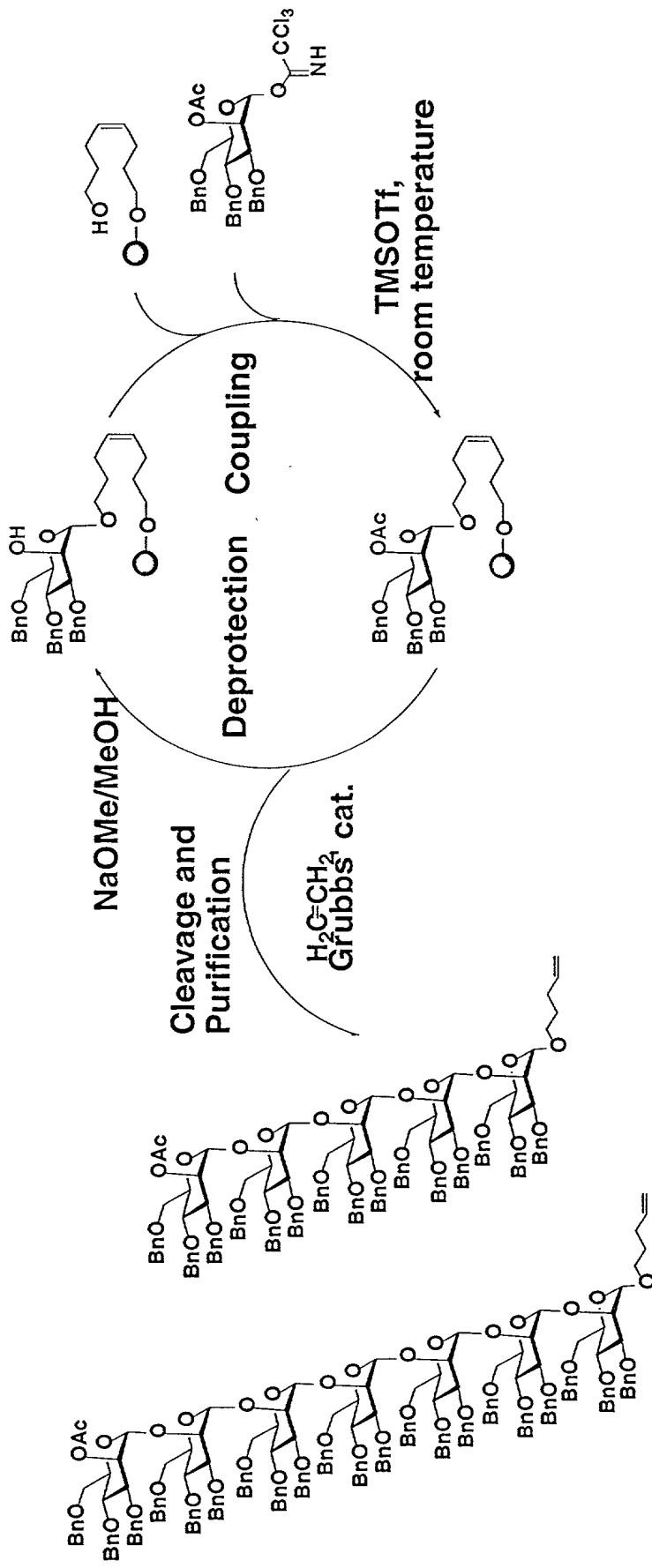
Automated Oligomannoside Synthesis: Coupling Cycle

	Reagent/Solvent	Equivalents	Time
Coupling	Donor TMSOTf	10 0.5	30 min
Washing	CH_2Cl_2 THF		5 min
Coupling	Donor TMSOTf	10 0.5	30 min
Washing	CH_2Cl_2 THF		5 min
Deprotection	NaOMe		30 min
Washing	CH_2Cl_2 THF		5 min
Deprotection	NaOMe		30 min
Washing	CH_2Cl_2 THF		5 min
Cycle Time per residue			140 min
25 μmol Scale			

Figure 15

Solid-Phase Oligosaccharide Synthesis: Coupling Cycle Development

Figure 16

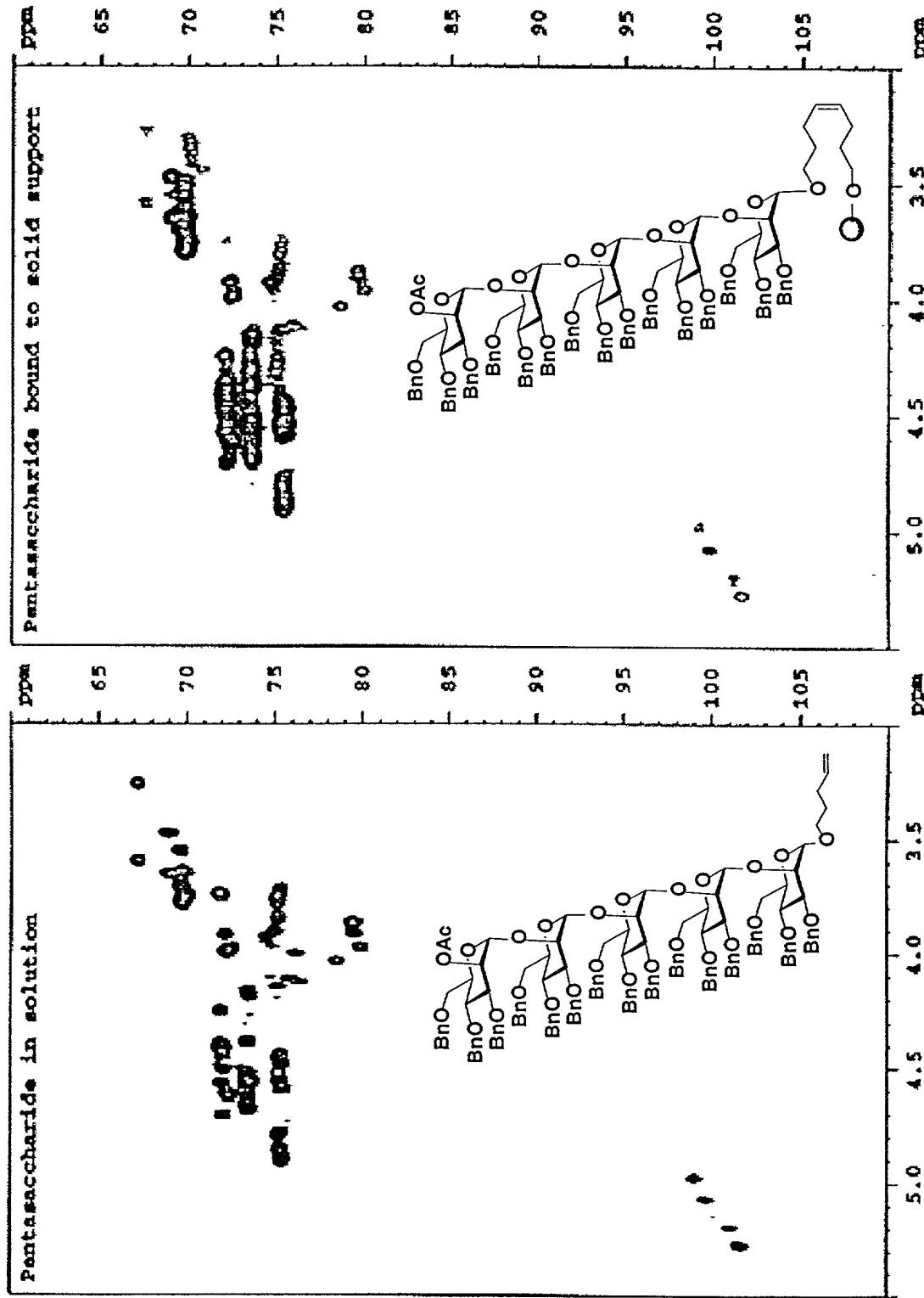


(manual synthesis: 9%)

stepwise yield: 94% stepwise yield: 94%

HR-MAS HMQC-Analysis of Pentamannosides

Figure 17



HPLC Purification of the Heptamannoside

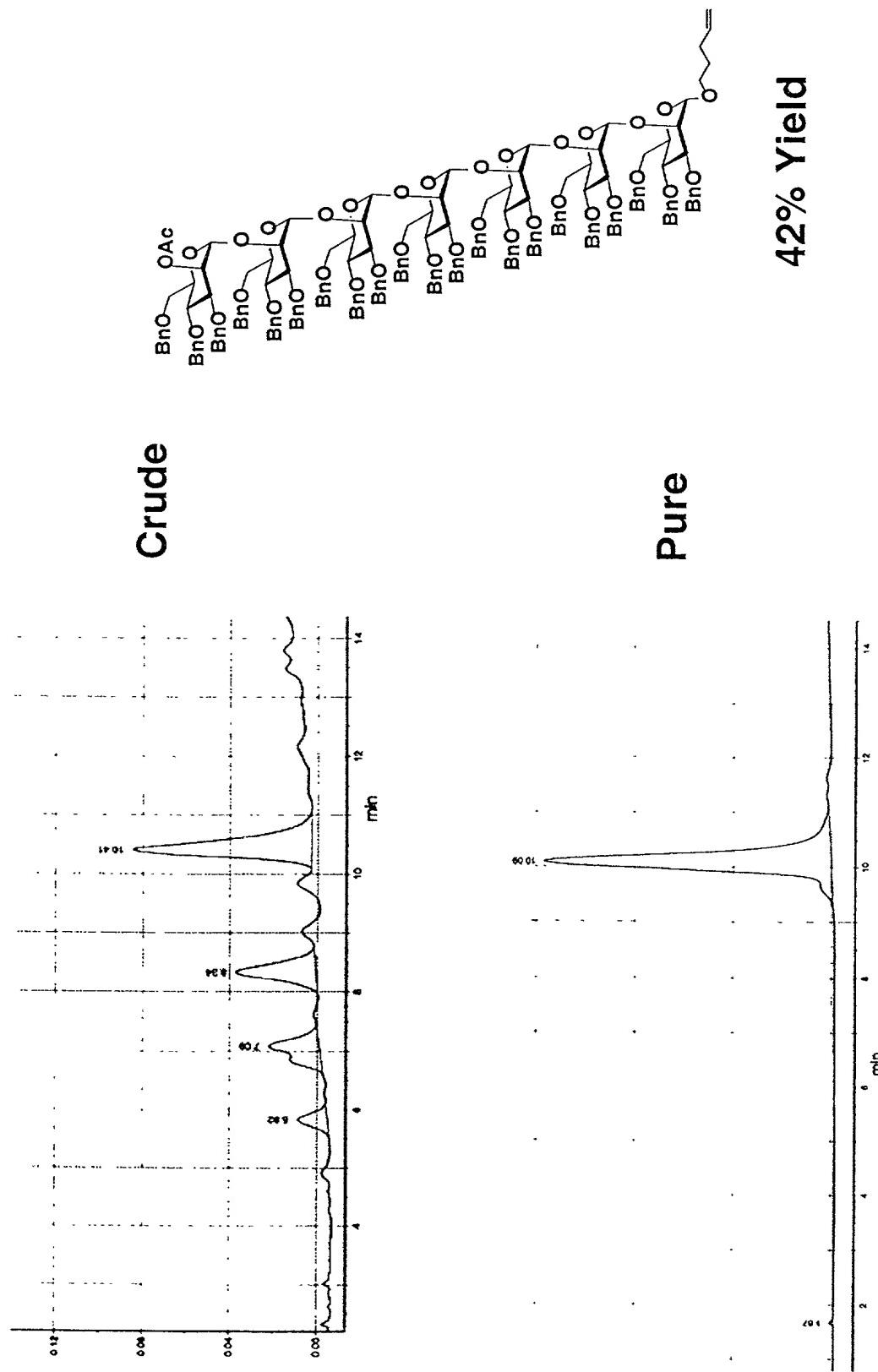


Figure 19

Automated Synthesis of a Decamannoside Using Trichloroacetimidates

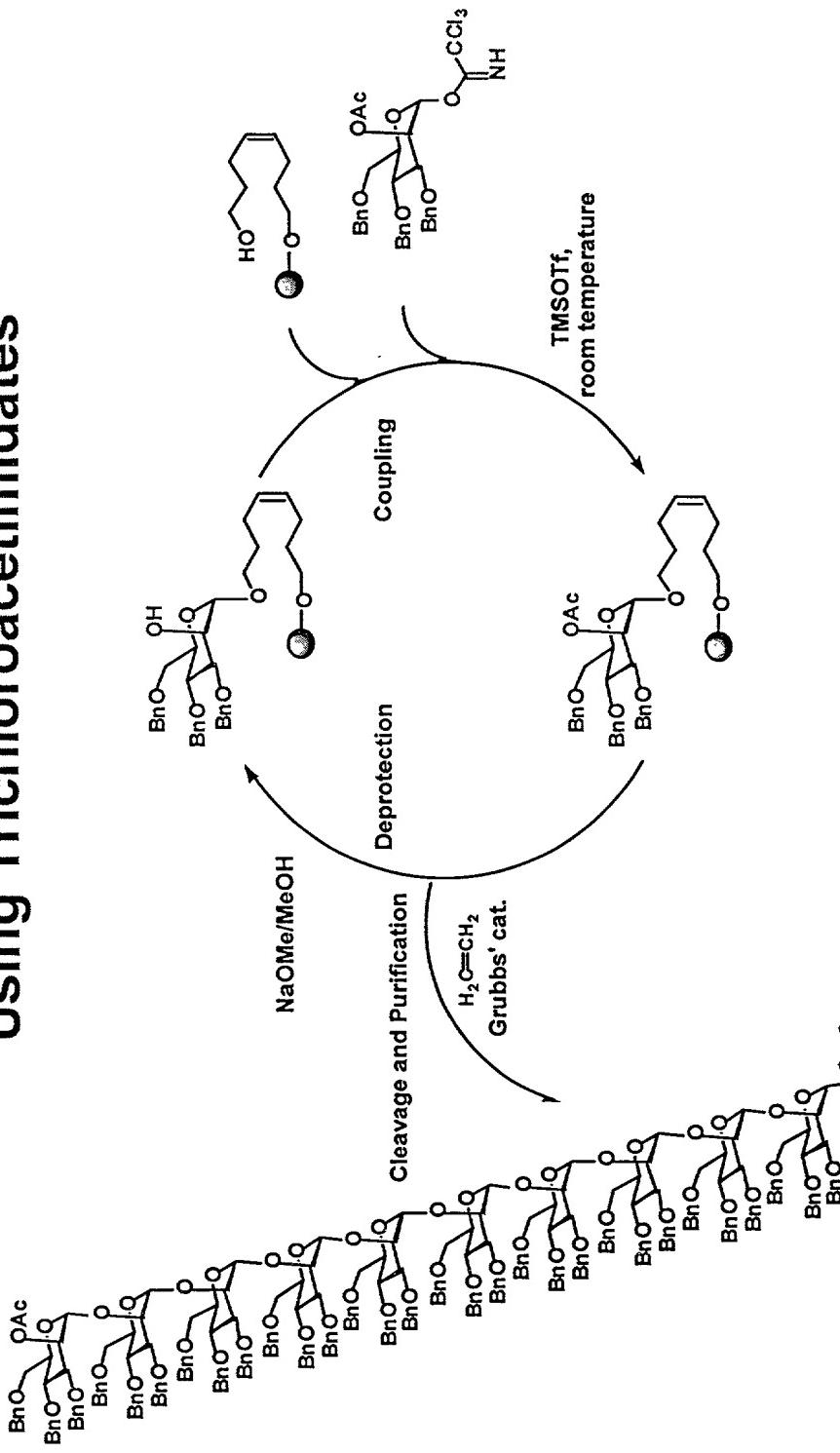


Figure 20

Automated Synthesis of Leishmania Cap Tetrasaccharide

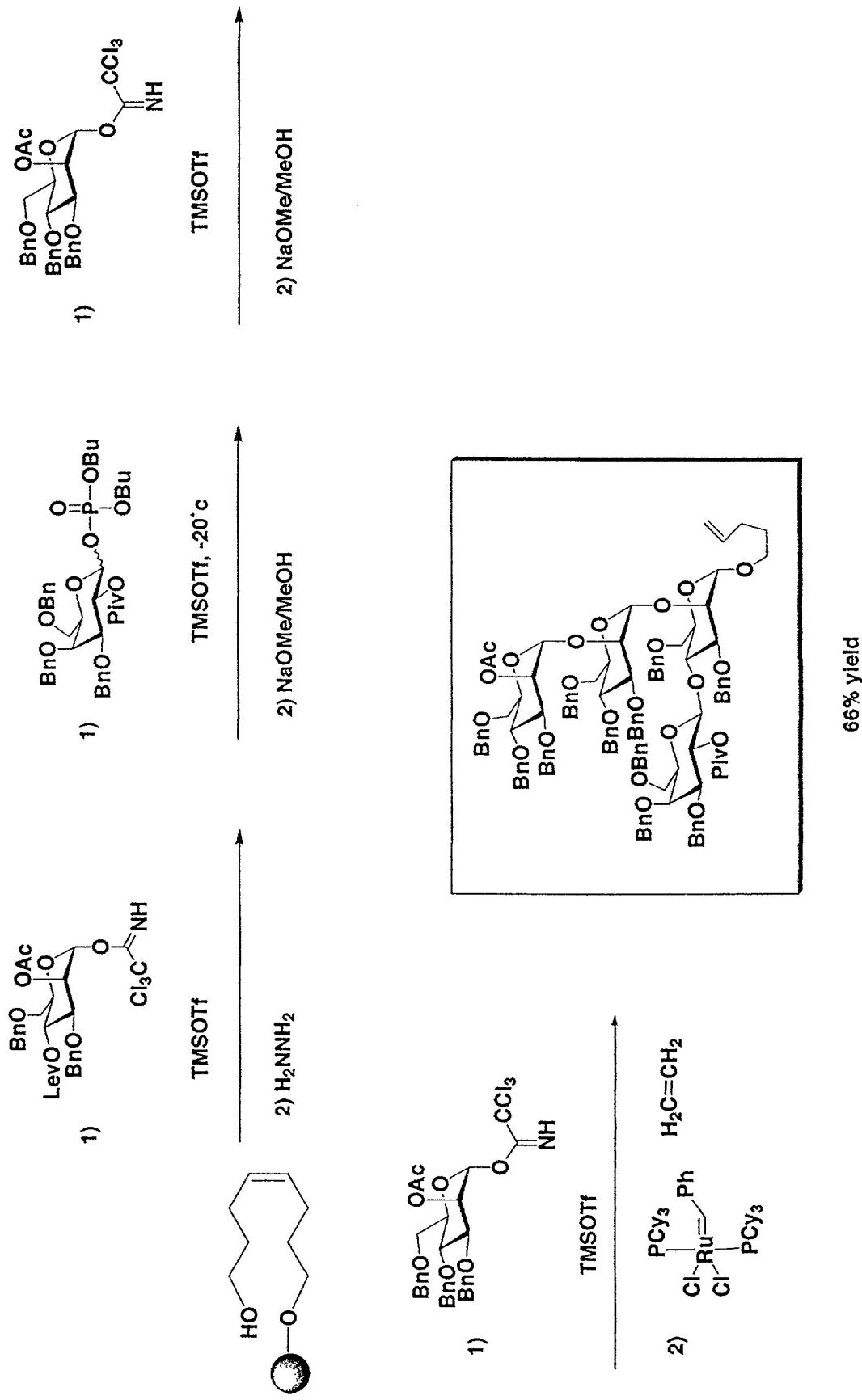
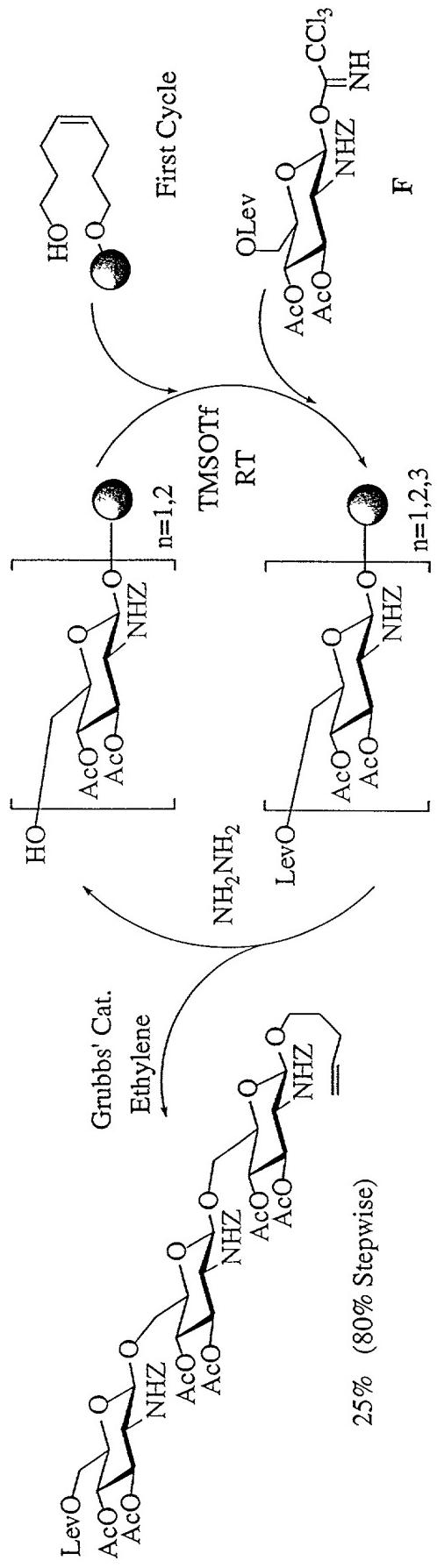


Figure 21

Automated Synthesis of GlcA Trisaccharide



Cycle:

Time: 8.5 h

Donor: 5.0 eq

Activator: 0.5 eq TMSOTf

Deprotection: 0.5 M $\text{NH}_2\text{NH}_2 \bullet \text{H}_2\text{O}$

Automated Synthesis of polyglucosamines

Figure 22

